

REMARKS**I. Disposition of Claims**

Applicants have canceled claims 11-13, 14, 15-25, 34, and 36-39. Cancellation of these claims do not change matters of inventorship.

II. Drawings

Examiners rejections have been noted and Applicants have corrected separately changes to drawings, by forwarding corrected drawings to the Drawing Review Branch.

III. Claim rejection-35 U.S.C. § 112

Claims 1, 2, 9, 26, 27, and 34 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that all claims are referring to "inhibiting the presence of DNA methylation". Inhibiting implies the stopping of a metabolic process. Usually this is accomplished by the introduction of a compound that has an inhibiting effect. The Examiner states, in this case, "inhibiting the presence of DNA methylation" is actually referring to the selection of those cells in which the "helper virus" is not inserted into a region of the genome that is hyper-methylated, thereby allowing for better transcription of the "helper virus" genes. Therefore, this is not the same as actively interfering with the methylation process by the addition of an inhibitor. Therefore, selection of clones that are not methylated does not equate to inhibiting methylation.

Applicants have amended claims 1, 2, and 9 from "inhibiting the presence of DNA methylation" to --eliminating the presence of DNA methylation-- to refer to the selection with an agent that eliminates cell with methylated helper virus from the population (Claim 2), which ensures sustained helper virus gene expression, which increases virion production. Support for this amendment can be found on page 23, lines 21-25; page 30, lines 20-25; and page 37, lines 35-37.

IV. Claim rejection

In claims 1, 9, 10, and 14 the Examiner states it is not clear if Markush claim format was intended in claims 10 and 14.

Applicants have amended claim 10 by removing the Markush claim format and have canceled claim 14, thus alleviating this rejection. Claims 1 and 9 are believed to be in proper format. Applicants request reconsideration.

V. Claim rejection-35 U.S.C. § 112

Claim 1 in all dependent claims were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the base claim.

(a) The Examiner states it is not clear what applicant intends by “sufficiently increasing”. This implies that the method must be compared to another method, yet the claim provides no insight as to which methods are compared in order to make a qualitative assessment that something is “sufficiently increased”.

Applicants have amended the claim by deleting any reference to “sufficiently increasing” thus alleviating this rejection.

(b) The Examiner questions whether “genome sequence viral structural proteins” is referring to the helper virus comprising viral structural proteins.

Applicants have amended claim 1 from “genome sequence viral structural proteins” to “retroviral structural genes” to clarify that this is referring to the helper virus construct. Support for this amendment can be found on page 11, line 27 and page 22, line 12 of the specification.

(c) The Examiner states that from the recitation “and a nucleotide sequence” it is not clear what nucleotide sequence is being referred to.

Applicants have amended the claim by removing the recitation “and a nucleotide sequence”, thus alleviating this rejection.

(d) Next, the Examiner states with regards to the recitation “capable of expressing an introduced viral components”, grammatical inconsistencies.

Applicants have amended the claim by deleting this recitation thus alleviating this rejection.

VI. Conclusion

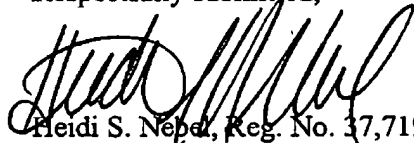
For the foregoing reasons, it is respectfully submitted that the proposed amendments be entered, and with their entry, the application is now in condition for allowance.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



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Application No. P04014US1

**AMENDMENT — VERSION WITH MARKINGS
TO SHOW CHANGES MADE**

In the Claims

Please cancel claims 11-13, 14, 15-25, 34 and 36-39.

Please amend claims 1, 2, 9, 10, and 27.

1. (Twice Amended)

A method for establishing a vector packaging cell line [and sufficiently increasing the production of viral vector titer in the vector packaging cell] with favorable vector packaging efficiency comprising:
introducing a helper virus into a cell to establish a packaging cell line, said helper virus comprising [a genome sequence viral structural proteins] retroviral structural genes in combination with an internal ribosome entry site [with] linked to a selection marker [and a nucleotide sequence, the presence of which enables a host cell to be capable of expressing an introduced viral components to form a viral particle so that said viral vector may be assembled into the viral particle to form an infectious viral particle]; and [increasing the vector production by inhibiting the presence of DNA methylation of helper virus in said cell] eliminating cells with methylated helper virus thereby increasing virion production.

2. (Twice Amended)

The method of claim 1 wherein said step of [inhibiting the presence of DNA methylation] eliminating cells with methylated helper virus comprises:
positively selecting helper virus which is functional.

9. (Twice Amended)

The method of claim [1] 3 wherein said [step of decreasing inactive helper virus comprises the step of:
inhibiting the presence of DNA methylation of helper virus in a cell] selection eliminates cells with methylated 5' LTR.

10. (Amended)

The method of claim [9] 1 wherein said [inhibiting] elimination [of methylation] is accomplished by[: a step of selected from the group consisting of:] treating [of] vector producer cells with 5-AZA-C.

27. (Amended)

A method of claim 26 wherein said step of [decreasing] eliminating inactive helper virus comprises the step of:
[inhibiting] eliminating methylation of helper virus.